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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,335	06/28/2004	Gerard Moinet	MERCK-2895	8953

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MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER	
ZHANG, NANCY L	
ART UNIT	**PAPER NUMBER**
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/26/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,335	MOINET ET AL.	
	Examiner	Art Unit	
	Nancy L. Zhang	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *4 and 10-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1 sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of Group I, claims 1-9, drawn to a composition comprising one α-glucosidase inhibitor and a compound of formula (I), along with acarbose as the α-glucosidase inhibitor, the compound (+) 2-benzyl-4-(4-fluorophenyl)-4-oxobutanoic acid and the disease of non-insulin-dependent-diabetes as the elected species, in the reply filed on 11/27/2006, is acknowledged. The traversal is on the ground that there would be no burden in searching for all pending claims. This is not found persuasive because the pending claims are directed to inventions of Group I and Group II which are distinctive, each from the other for the reason of the record. Furthermore, the search of the entire groups in the non-patent literature (a significant part of a thorough examination) would be burdensome. The requirement is deemed proper and is therefore made FINAL.

Claims 10-16 are withdrawn from consideration because they are not directed to the elected invention.

Claim 4 is withdrawn from consideration because it is not directed to the elected species.

Claims 1-3 and 5-9 are examined.

Claim Objections

Claim 1, 6-8 are objected to because of the following informalities:

The use of Markush group in claims 1, 6-8 is improper. The phrase "chosen from" should be changed to "chosen from the group consisting of". The items in a

Markush group should be linked by commas and the conjunction of "and" should be used to link the last two items in the Markush group.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3 and 5-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 1, the recitation of the limitations for groups A and B is unclear. The recitation of "the groups A and B" in line 14 of claim 1 renders the claim indefinite because it is unclear what "the groups A and B" in line 14 of claim 1 is referring to. "the groups A and B" in line 14 of claim 1 is part of a selection list that defines "the groups A and B" in line 6 of claim 1 for formula (I) and should not refer back to "the groups A and B" in line 6 of claim 1 for formula (I).

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then

narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 5 recites the broad recitation "ranges from 10^{-3} to 40", and the claim also recites "ranges from 10^{-3} to 30" and ""ranges from 10^{-3} to 30"" which are the narrower statements of the range/limitation.

Scope of Enablement Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5 and 7-9 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition comprising α-glucosidase inhibitors such as acarbose, miglitol, voglibose and emiglitate and a compound of formula (I), does not reasonably provide enablement for a pharmaceutical composition comprising any α-glucosidase inhibitor and a compound of formula (I). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The instant claims are drawn to a pharmaceutical composition comprising "an α-glucosidase inhibitor" and "a compound of formula (I)".

The relative skill of those in the art of pharmaceuticals and the unpredictability of the pharmaceutical art is very high. In fact, the courts have made a distinction between mechanical elements function the same in different circumstances, yielding predictable results, chemical and biological compounds often react unpredictably under different circumstances. Nationwide Chem. Corp. v. Wright, 458 F. supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); In re fischer, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970). Thus, the physiological activity of a chemical or biological compound is considered to be an unpredictable art.

Given the broadest reasonable interpretation of the claims, the recitation of claims 1-3, 5 and 7-9 includes any compound that is "an α-glucosidase inhibitor". The claims are very broad due to the unlimited number of possible compounds having the

characteristic as being "α-glucosidase inhibitors". The scope of the claimed invention covers "compounds capable of inhibiting α-glucosidase" that are known to exist and those that may be discovered in the future, for which there is no enablement provided.

Although the specification discloses acarbose, miglitol, voglibose and emiglitate as the preferred "α-glucosidase inhibitor", the specification fails to provide how to make and screen "a compound capable of inhibiting α-glucosidase" encompassed by the instant claims without undue amount of experimentation. As discussed in preceding comments, in the instant case, only a limited number of "α-glucosidase inhibitors" are set forth in the specification. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The instant claims read on any compounds having "capable of inhibiting α-glucosidase", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

As discussed in preceding comments, to practice the instant invention to the claimed scope, applicant would have to make or screen numerous potentially suitable compounds characterized as "α-glucosidase inhibitor". In other words, the instant invention necessitates for the skilled artisan to undergo an exhaustive search for the embodiments suitable to practice the invention as claimed in claims 1-3, 5 and 7-9.

Given the breadth, the disparate nature of compounds that is presently claimed, the highly unpredictable state of the art where many specific differences or different physicochemical properties are existed among unrelated structural compounds or even structurally related compounds, the limited number of working examples and the

insufficient amount of guidance present in the specification, one of ordinary skill in the art would have to undergo an undue amount of experimentation to practice the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 and 5-9 are rejected under 35 U.S.C. 103(a) as being obvious over Tsukada et al. (US Patent 5,840,705, issue date: Nov. 24, 1998) in view of Moint et al. (US Patent 6,143,787, issue date: Nov. 7, 2000).

Claims 1-3 and 5-9 are drawn to a composition comprising, as active principles, (i) one α-glucosidase inhibitor such as the elected agent acarbose and (ii) a compound

of formula (I) such as the elected compound (+) 2-benzyl-4-(4-fluorophenyl)-4-oxobutanoic acid. Further limitations include: the composition is for treating non-insulin-dependent-diabetes (NIDDM) (claim 3); the weight ratio of α-glucosidase inhibitor and the compound of formula (I) ranges from 10^{-3} to 40 (claim 5); and the pharmaceutical composition is suitable for oral administration (claim 9).

Tsukada et al. disclose that acarbose is an α-glucosidase inhibitor that has been applied as an oral therapeutic agent for treating NIDDM (column 1, lines 45-47).

The difference between the prior art teaching and the instant invention lies in that the prior art does not teach the combined use of acarbose with a compound of formula (I) in a composition for treating NIDDM.

However, Moint et al. teach that compounds of the formula (I) such as 2-benzyl-4-(4-fluorophenyl)-4-oxobutanoic acid (column 2, line 2) are useful in treatment of diabetes, in particular insulin-independent diabetes (NIDDM) (column 3, lines 59-60) and may be provided in forms intended for oral administration (column 3, line 64).

In re Kerkhoven (205 USPQ 1069, CCPA 1980) states that "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the same purpose: the idea of combining them flows logically from their having been individually taught in the prior."

Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine the antidiabetic agent acarbose and the antidiabetic compound 2-benzyl-4-(4-fluorophenyl)-4-oxobutanoic acid in a 1/1 weight

ratio for treating NIDDM to result in the pharmaceutical composition of the instant invention with a reasonable expectation of success, motivated by their having been taught by the prior art to be useful in treating NIDDM, consonant with the reasoning of the cited case law.

With respect to the recitation of claim 8 where the enantiomers of 2-benzyl-4-(4-fluorophenyl)-4-oxobutanoic acid are used in the pharmaceutical composition, although enantiomers of one compound may have substantially different biological effects, one of ordinary skill in the art would expect enantiomers of a compound as having similar activities, in absence of any evidence to the contrary. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the instant invention to use an enantiomer of the antidiabetic compound 2-benzyl-4-(4-fluorophenyl)-4-oxobutanoic acid in combination with the antidiabetic agent acarbose in a composition as discussed above for treating NIDDM with the expectation that the enantiomer of the antidiabetic compound would also have the same properties in treating NIDDM due to the fact that their chemical structure is the same.

With respect to the dosage weight ratio of between α-glucosidase inhibitor and the compound of formula (I), the determination of the appropriate dosage amounts of active ingredients for a treatment is routinely made by those of ordinary skill in the art and is well within the ability of tasks routinely performed by them without undue experimentation. Thus, it would have been obvious to one of ordinary skill in the art at the time the instant invention was made to determine the amount of α-glucosidase inhibitor and the amount of the compound of formula (I) for achieving the additive effects

of treating NIDDM to result in the pharmaceutical composition as claimed with a reasonable expectation of success.

Applicant's attention is further drawn to MPEP at §2144.05, which states, "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage range is the optimum combination of percentages... Where the general condition of a claim are disclosed in the prior, it is not inventive to discover the optimum or workable ranges by routine experimentation."

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy L. Zhang whose telephone number is (571)-272-8270. The examiner can normally be reached on Mon.- Fri. 8:30am - 5:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NLZ 12/15/06

NLZ

BRIAN-YONG S. KWON
PRIMARY EXAMINER